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VOLPE AND KOENIG, P.C.
SUITE 400, ONE PENN CENTER
1617 JOHN F. KENNEDY BOULEVARD
PHILADELPHIA, PA 19103

EXAMINER
GOLDBERG, JEANINE ANNE

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/872,063	LO ET AL.	
	Examiner	Art Unit	
	Jeanine A Goldberg	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 May 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23 and 31-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23 and 31-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is in response to the papers filed May 13, 2002. Currently, claims 1-23, 31-36 are pending. All arguments have been thoroughly reviewed but are deemed non-persuasive for the reasons which follow. This action is made FINAL.

2. Any objections and rejections not reiterated below are hereby withdrawn.

3. This action contains new grounds of rejection necessitated by amendment.

4. It is noted that the IDS filed May 13, 2002 contains several entries which have been lined through either because they have already been cited on an 892 or because the information contained in the citation does not include the necessary information including author, date, publication, volume, pages, etc.

New Matter

5. Claims 1-5, 16-19, 22-23, 33, 36 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In the amended claims, references to "detecting the presence of a fetal nucleic acid which differs from that of the maternal genome" are included. The amendment states that the change is for clarification purposes only and is no way connected to the art. However, the specification does not describe or discuses "detecting the presence of a fetal nucleic acid which differs from that of the maternal genome". The response on

page 7, indicates the continuing application is seeking to obtain claims which more fully reflect the generality of the invention. The response has broadened the claims from paternally interited, which was patented, to detecting the presence of a fetal nucleic acid which differs from that of the maternal genome, because the term "paternally inherited" dies not cover the cases where (a) the gene is maternally inherited, yet is not the same as the fetus as in the mother and (b) the gene is altered spontaneously. The specification does not encompass these two situations in which applicant is seeking to protect. Instead the specification describes "determination of any maternal or fetal condition or characteristic which is related to either the fetal DNA itself or to the quantity or quality of the fetal DNA in the maternal serum or plasma" (page 3 of specification). The specification further describes the method can be applied to the detection of any paternally-inherited sequences which are not possessed by the mother and which may be for example gene which confer a disease phenotype in the fetus (page 4). This description does not support detecting the presence of a fetal nucleic acid which differs from that of the maternal genome. While the concept of detecting fetal nucleic acids which are paternally inherited in maternal serum/plasma, the specification does not support the concepts of either nucleic acids which differ between maternal genome and fetal genome and spontaneous differences. The concept of "detecting the presence of a fetal nucleic acid which differs from that of the maternal genome" does not appear to be completely supported as part of the originally filed invention. The specification does not appear to have contemplated either spontaneous alterations in the egg and sperm nor differences between maternal and fetal nucleic acids which are argued to be

encompassed by the instant claims. Therefore, "detecting the presence of a fetal nucleic acid which differs from that of the maternal genome" constitutes new matter.

Moreover, Claim 36 has been added which includes "performing analysis on maternal serum or plasma sample from a pregnant female by isolating fetal cells and detecting the presence of fetal cells". The instant specification is not directed to detecting fetal cells in maternal serum or plasma. The instant specification is directed to detecting nucleic acids in maternal serum or plasma. There is no teachings in the specification regarding isolating fetal cells from the serum or plasma. Moreover, as provided in the medical dictionary, plasma is defined as "acellular fluid in which blood cells are suspended." http://www.medical-dictionary.com/. Blood serum is defined as the clear liquid that separates from blood on clotting. Moreover, blood plasma has also been defined as "this is whole blood minus the cells"; and serum is defined as "the liquid portion of blood left over after all of the cells have been removed" http://biotech.icmb.utexas.edu/search/dict-search.html. Therefore, the concept of isolating fetal cells from maternal serum and plasma is not supported by the definition of either serum or plasma nor by the instant specification.

Applicant is required to cancel the new matter in the reply to this Office Action.

Maintained Rejections

Priority

6. This application is a continuation of 09/380,696, filed November 29, 1999, now patent US Pat. 6,258,540 and a 371 of GB98/00690, filed March 4, 1998. This application also claims priority to GB9704444, filed March 4, 1997.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Newly amended Claims 1-23, 31-32 and Newly added Claims 33-36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for detecting a paternally inherited nucleic acid of fetal origin performed on a maternal serum or plasma sample from a pregnant female, which comprises amplifying a paternally inherited nucleic acid from the serum or plasma sample and detecting the presence of a paternally inherited nucleic acid of fetal origin in the sample, does not reasonably provide enablement for a detection method performed on serum or plasma for detecting fetal nucleic acid in general. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to us the invention commensurate in scope with these claims.

The claims are broadly drawn to a detection method performed on serum or plasma of a pregnant woman to detect any fetal DNA at any point in pregnancy.

The specification teaches fetal DNA has been detected in both serum and plasma. Table 2 and 3 show the quantification of fetal DNA in maternal serum and plasma in relation to the gestational age (pg. 33). The specifications teaches the detection of the Y-chromosome by markers to DYS14 locus and SRY gene. The specification teaches that plasma and serum samples were collected from 43 pregnant women with gestational ages from 12 to 40 weeks (pg. 9, para. 1). Of the 30 male fetuses, detection of a Y-positive signal occurred in 24 plasma samples and only 21 serum samples (pg. 9,para. 1). The specification also teaches a RhD status determination from plasma of RhD-negative pregnant women (pg. 15 and Table 1, pg. 20). The specification teaches that the DNA detected is paternally inherited (page 4, para 18) and requires amplification.

The art teaches unpredictability in detecting fetal DNA in plasma before the 15th week of gestation, of detecting paternally inherited non-Y sequences, and the unpredictability of detecting fetal DNA in serum samples. Specifically, Lo et al (New England J. of Med. , Vol. 339, No. 24, pages 1734-8, December 1998) teaches reliable results for fetal RhD status determination were obtainable from the 15th week of gestation and beyond in RhD negative women. Lo teaches that 7 of 9 fetus were positive on PCR testing for RhD genotyping (Table 1, pg. 1736). Lo teaches that two women with gestation ages of eight and nine weeks yielded false negative results (pg. 1735, col. 2, para. 6). Lo explicitly states "our data suggests that results of the RhD PCR test are reliable beginning in the second trimester" (pg. 1736, col. 2, para. 2). Additionally, Lo (Annals of Medicine, Vol. 31, NO. 5, pg. 308-312, Oct 1999) teaches "it

is likely that future improvements in technology may allow more accurate diagnosis to be made and potentially extend the applicability of this method to the first trimester of pregnancy" (pg. 310, col. 2, para. 1) suggesting that the technology does not currently exist and may not have been conceived of as of yet what would be required to diagnose in the first trimester.

Moreover, the art teaches the detection of fetal DNA in maternal plasma for an expanded CGT trinucleotide repeats, in the DM kinase gene on chromosome 19, in the range of 50-4000 repeats (Amicucci et al, February 2000, Clinical Chemistry, Vol. 46, No. 2, pages 301-302). Amicucci teaches sampling of plasma from pregnant women at 10 weeks of gestation to detect the expanded repeat present only in the father. Amicucci states "at present, this test seems appropriate only for monitoring paternally inherited expanded alleles" (pg. 302, para. 2). Additionally, Lo (Annals of Medicine, Vol. 31, NO. 5, pg. 308-312, Oct 1999) states "the success of the detection of fetal-derived RhD gene in the plasma and serum of pregnant women opens up the possibility that a similar approach may be used for other single-gene disorders" (pg. 310, col. 2, para. 3). However, Lo has not taught single gene disorders other than RhD which may in fact use this technique. Furthermore, the RhD analysis was only shown to be successful on RhD-negative women. The language of the paper is that of suggestion, and hypothesis rather than of evidence that this method works for these suggested single-gene disorders.

The art provides a summary of the state of the art (Pertl et al. Obstet Gynecol, Vol. 98, No. 3, pages 483-90, September 2001). Pertl et al (herein referred to as Pertl)

teaches that a search was conducted of the art from 1970-2000 and provides a summary of the state of the art. Pertl teaches that the "diagnostic use of circulating fetal DNA in maternal plasma is currently limited to genes that are present in the fetus but not in the mother". Further, discussion of the effectiveness of the analysis beginning in the second trimester is provided. Pertl suggests that "the main limitation at present appears to be the availability of uniquely fetal gene sequences that will identify the presence of fetal DNA in both male and female fetuses" (page 484). Pertl teaches that fetal DNA has been detected by PCR amplification and a real-time quantitative PCR assay. Pertl also discusses the detection of fetal aneupoidy, such that "this method can be applied only to a very small number of paternally inherited fetal aneuploidies. Furthermore, the selected markers must be informative, with both paternal alleles sizes differing from those of the mother." (page 487, col. 2).

Neither the specification nor the art provides guidance to overcome the unpredictability of detecting fetal DNA in plasma before the 15th week of gestation, of detecting non-paternally inherited sequences. It would require undue experimentation for the ordinary artisan to practice the invention as broadly as claimed. The concentration of fetal DNA in maternal plasma at early stages of gestation appears to be low. Thus predictably detecting fetal DNA in maternal plasma samples before the 15th week of gestation is unpredictable and would require the ordinary artisan to enrich the fetal DNA in some manner which have not been described such as PCR amplification. The specification does not provide any information as to the quantity of fetal nucleic acids present during the first trimester of pregnancy. It is highly

unpredictable as to whether sufficient quantities of fetal nucleic acids are present in maternal serum or plasma during the first trimester of pregnancy as to allows for the specific detection of fetal nucleic acids. It is unpredictable that the fetal nucleic acids could be detected without first amplifying the fetal nucleic acids.

The detection of a maternally inherited nucleic acid from the fetus is unpredictable. The specification explicitly states that "the method of the invention can be applied to the detection of any paternally-inherited sequences which are not possessed by the mother" (pg. 4, lines 5-7). As stated in numerous of the papers the concentrations of fetal DNA in maternal plasma may reach 3.4% in early pregnancy and 6.2% in late pregnancy, however, there is a much higher percentage of maternal DNA in the plasma. Provided that the skilled artisan obtained a positive result for detection of the nucleic acid, it would require undue experimentation determine whether the nucleic acid was a results of the maternal DNA found in the maternal plasma or whether in fact the nucleic acid was from the fetus. The specification does not provide any teachings nucleic acids which are specific to the fetus and absent in the maternal serum/plasma. Thus, detection of a maternally inherited nucleic acid would be unpredictable and require undue experimentation.

With respect to claim 5, applicant has not provided that one would be able to, without unpredictability, detect fetal nucleic acid by merely taking a sample of serum or plasma with a sequence specific probe. Applicant has illustrated the need for amplification or purification. The background within serum and plasma of maternal DNA in addition to other elements would be very high.

With respect to Claim 12, applicant has not provided any guidance to the skilled artisan to practice the claim without unpredictability. The specification describes detection of RhD and Y chromosome. The specification does not provided detection of a disease phenotype. It is unpredictable that a disease phenotype which occurs due to a single point mutation would be detectable.

With respect to Claim 31, the claim is broadly drawn to a method of prenatal diagnosis for a condition which comprises obtaining a serum/plasma sample and determine the presence or absence of one or more selected nucleic acid sequence in the detected fetal nucleic acid. The absence of a sequence it not supported. As stated above, it is unpredictable without amplification or enrichment that the lack of detection is indicative of the lack of the presence. Further, applicants have only illustrated paternally inherited nucleic acids.

Thus, the above analysis demonstrates that the skilled artisan would be required to perform undue experimentation to make and use the invention as claimed.

Response to Arguments

The response traverses the rejection. The declaration filed under Rule 132 by Professor Lo has been thoroughly reviewed and considered. The response asserts that the inventors had conceived their invention as applicable to the first trimester of pregnancy, i.e. before the 15th week of gestation. This argument has been reviewed but is not convincing because each of these references which are directed to early pregnancy detection of fetal nucleic acid sequences has required amplification. Therefore, based upon the teachings in the art and in the declaration filed by Professor

Lo, detection in the first trimester requires amplification. Professor Lo states, section 4, "I believe that those familiar with DNA amplification techniques would be able to achieve useful results from samples taken during the first trimester of pregnancy". Moreover, the papers by Faas, Sekizawa, Honda, Amicucci each perform amplification steps on the plasma/serum prior to analysis. Therefore, without amplification, it is unpredictable to detect fetal nucleic acids in the first trimester. The quantity of fetal nucleic acid in the serum/plasma of the mother is small. The specification teaches "the fractional concentration of fetal DNA in early pregnancy ranges from 0.39% to 11.9% (mean: 3.4%) in plasma and 0.014% to 0.54% (mean 0.13%) in serum" (page 27). This concentration of fetal DNA in serum and plasma is very small. Therefore, in order to detect the nucleic acids, each of the cited references and instant specification has used amplification to obtain detectable levels of nucleic acids in early pregnancy samples.

The response asserts that it is immaterial whether the DNA detected is paternally inherited or not (page 9 of response filed May 13, 2002). This argument has been thoroughly reviewed and considered. It is noted that detection of nucleic acids in samples do not necessarily need to be paternally inherited. However, in order to conclude that the detected nucleic acid is of fetal origin, the nucleic acid could not also be present in the maternal genome. For the reasons above, in the new matter rejection, the instant specification does not appear to be directed to spontaneous mutations or to differences between maternal and fetal DNA. The specification discusses the paternally inherited DNA.

The response, on page 13, asserts that detection of maternally inherited nucleic acids is not unpredictable. The response argues that it is immaterial how such a fetal sequence arises. This argument has been reviewed, but is not persuasive. It is not unpredictable to detect a mutation in a nucleic acid which is found in the maternal genome. It is unpredictable whether the nucleic acid on which the mutation or alteration was found is a fetal nucleic acid. The maternal serum/plasma contains not only fetal DNA but also maternal DNA. Therefore, detection of a nucleic acid in the maternal serum/plasma does not indicate that the nucleic acid found is fetal DNA.

The response traverses the rejection, page 16, as it applies to detecting the absence of a sequence. While the specification has indicated that the absence of a Y chromosome sequence is indicative of a female fetus, this single example does not support the full scope of the claims which is directed to determining the absence of a nucleic acid sequence as indicative of a fetal genetic condition. For example the absence of a particular mutation does not indicate that the fetus does not have the condition for those conditions which may be affected by more than one nucleic acid.

With respect to the need for amplification as an essential method step, applicants assert that "whilst it may be preferable to use an amplification technique, this is not a limitation of the method of the invention" (page 10 of response filed May 13, 2002). The response cites a post filing date reference, Poon, to illustrate the detection of fetal DNA carried out on maternal plasma obtained at 12 &15 and 15 and 21 weeks using a probe (page 11, of response filed May 13, 2002). Poon has been thoroughly reviewed. The instant specification makes clear that serum and plasma do not contain cellular fractions

(page 7 and 28, for example, Example 1). Poon appears to be directed to illustrating that prenatal detection of fetal trisomy 21 can be accomplished by FISH analysis of fetal cells harvested from maternal plasma (page 1820, col 1). Poon analyzes cells obtained from diluted maternal blood with PBS, centrifugation, washing and fixation. Therefore, isolation of cells and subsequent analysis is not analogous to detection in the plasma and serum liquid as supported by the instant application.

Thus for the reasons above and those already of record, the rejection is maintained.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1, 5-16, 18-23, 31-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1, 5-16, 18-23, 31-35 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: amplification of the nucleic acids. With out the amplification step, there appears to be a gap between the sample and the detection step.

Response to Arguments

The response traverses the rejection. The response asserts that amplification is not an essential step. This argument has been reviewed but is not convincing because

the response has not demonstrated that amplification is not an essential step for the method, as provided above. Thus for the reasons above and those already of record, the rejection is maintained.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 1-32 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-27 of U.S. Patent No. 6,258,540, July 10, 2001. Although the conflicting claims are not identical, they are not patentably distinct from each other. The claims of the instant application are drawn to methods of detecting fetal DNA in a sample from maternal serum or plasma. The claims of patent 6,258,540 are drawn to methods of detecting paternally inherited DNA of fetal origin by amplifying the paternally inherited nucleic acid from plasma or serum and detecting the presence of the fetal DNA.

Response to Arguments

The response traverses the rejection. The response asserts that applicants intend to submit a terminal disclaimer when the other issues of Patentability are resolved. Thus for the reasons above and those already of record, the rejection is maintained.

10. Claims 1-32 provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-27 of copending Application No. 09/876,005. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of 09/876,005 are directed to methods for prenatal monitoring on a blood sample which does not contain anucleated cells and testing the sample for fetal RNA. While the claims of 09/876,005 are drawn to method which detect RNA, RNA is clearly within the genus of fetal nucleic acids. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

The response traverses the rejection. The response asserts that 09/876,005, filed June 6, 2001 is not commonly owned, and the Applicant's parent case is believed to be prior art. As provided in MPEP 800, Chart I-B for "different inventions, not patentably distinct", applications that have at least one common inventor, but no common assignee should be rejected as a provisional obviousness double-patenting rejection, a provisional rejection under 102(e) (if appropriate) and a rejection under 102(f) or 102(g). This argument has been reviewed but is not convincing. As provided

above, the doctrine of double patenting grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. The claims of 09/876,005 fall entirely within the scope of the instant claims. Namely the instant claims are drawn to nucleic acids. The Claims of the 09/876,005 application are drawn to RNA which is a nucleic acid. The instant specification teaches that nucleic acids encompass not only DNA, but also mRNA (page 3). Thus for the reasons above and those already of record, the rejection is maintained.

New Grounds of Rejection Necessitated by Amendment

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 31, 36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A1) Claim 31 is indefinite because it is unclear how the preamble is accomplished. Claim 31 is indefinite because the claims do not recite a positive process step which clearly relates back to the preamble. The preamble states that the method is for non-invasive prenatal diagnosis for determining a fetal genetic condition but the final process step is determining the presence or absence of one or more nucleic acid sequences. Therefore the claims are unclear as to whether the method is a method of

diagnosis of fetal genetic conditions or merely determining the presence or absence of nucleic acid sequences. It is unclear from the method how one would go from the detection of the presence of the nucleic acid to a diagnosis.

B1) Claim 36 is indefinite over the recitation "isolating fetal cells, from maternal plasma or serum" because based upon the definition in the art, both plasma and serum are cell free. As provided in the medical dictionary, plasma is defined as "acellular fluid in which blood cells are suspended." http://www.medical-dictionary.com/. Blood serum is defined as the clear liquid that separates from blood on clotting. Moreover, blood plasma has also been defined as "this is whole blood minus the cells"; and serum is defined as "the liquid portion of blood left over after all of the cells have been removed" http://biotech.icmb.utexas.edu/search/dict-search.html. Therefore, it is unclear how one would isolate cells from a cell free portion liquid.

Conclusion

12. No Claims allowable.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Enewold Goldberg whose telephone number is (703) 306-5817. The examiner can normally be reached Monday-Thursday from 7:00AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax number for this Group is (703) 305- 3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

J. Goldberg

Jeanine Enewold Goldberg
August 8, 2002

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600